Application No. 10/540,443

Reply to Office Communication Dated: January 25, 2008

Response Dated: March 7, 2008

Amendments To The Specification:

Please amend the Specification to read as follows:

Enter the Sequence Listing accompanying this submission into the Specification of the above-identified application.

Replace Table 1 in the Specification of the above-identified application with the following table:

Table 1. Naturally Occurring Opioid Peptide Sequences.

Peptide	Sequence	Subtype
Met-Enkephalin	YGGFM (SEQ ID NO:2)	μ/δ
Leu-Enkephalin	YGGFL (SEQ ID NO:3)	δ/μ
Dynorphin A	YGGFLRRIRPKLKWNNQ (SEQ ID NO:4)	κ(μ)
Dynorphin B	YGGFLRRQFKVVT (SEQ ID NO:5)	$\kappa(\mu,\delta)$
α-Neoendorphin	YGGFLRKY (SEQ ID NO:6)	к(μ,δ)
β-Neoendorphin	YGGFLRKYP (SEQ ID NO:7)	$\kappa(\mu,\delta)$
β_h -Endorphin	YGGFMTSEKSQTPLVTLFKNAIIKNAYKKGE (SEQ ID NO:8)	μ/δ
Peptide E	YGGFMRRVGRPEWWMDYQKRYGGFL (SEQ ID NO:9)	μ/κ
Peptide F	GGEVLGKRYGGFM (SEQ ID NO:10)	
Nociceptin	FGGFLRRIRPKLKWNNQ (SEQ ID NO:11)	ORL
Deltorphin	YmFHLMD-CONH ₂ (SEQ ID NO:12)	δ
Dermorphins	YaFGYPS-CONH ₂ (SEQ ID NO:13)	μ
Morphiceptin	YPFP-CONH ₂ (SEQ ID NO:[[14]] <u>12</u>)	μ
β-Casomorphin	YPFPGPI (SEQ ID NO:[[15]] <u>13</u>)	μ
Endomorphin-1	YPWF-CONH ₂ (SEQ ID NO:[[16]] 14)	μ
Endomorphin-2	YPFF-CONH ₂ (SEQ ID NO:[[17]] <u>15</u>)	μ
Rubiscolin-6	YPLDLF (SEQ ID NO:[[18]] <u>16</u>)	δ

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Replace paragraph [00018] in the Specification of the above-identified application with the following paragraph:

[00018] The classic motif for opioid receptor binding is the YGGF (SEQ ID NO:1) sequence. While some variations are possible in this motif, it appears that the first tyrosine and the fourth phenylalanine are invariant requirements of enkephalins. The discovery of natural opioid peptides in the skin of the frog *Phyllomedusa bicolor*, which naturally produces the enantiomeric D-amino acids, led to investigations of other D-amino acids which can substitute for the glycine intermediate residues in the motif. In particular, the several motifs with a D-amino acids, including Tyr-D-Cys-Gly-Phe (SEQ ID NO:19), Tyr-D-Ala-Gly-Phe (SEQ ID NO:20), and Tyr-D-Thr-Gly-Phe (SEQ ID NO:21) have been found effective synthetic enkephalin message sequences. Synthetic enkephalin analogues with a D-amino acid substituted for the first glycine have been designed to bias the conformation of the molecule to obtain greater affinity for opioid receptors. Note that in the Table 1 above and 2 below that the small case letter designation refers to a D-amino acid, such as "t" referring to D-Thr.

Application No. 10/540,443 Reply to Office Communication Dated: January 25, 2008 Response Dated: March 7, 2008 Replace Table 2 in the Specification of the above-identified application with the following table:

TABLE 2

				Receptor Binding Characteristics	g Chara	cteristi	S				
ID Code	Message		Address		Delta MU	MU	MVD	GPI	ICV(Mouse)	IV(Mouse)	+ Err (95%)
		(Transt	Transport Sequence)		nM	nM	ПМ	nM	IC50 nmol	umol/kg	umol/kg
Morphine	Morphin	Morphine Morphine	ine						2.7	6.3	4.9-7.9
SAM 995	YtGFL	S-CONH	YtGFL S-CONH2-(SEQ ID NO:22)	2)	2.1	7.5	2.723	25.04	0.07	46.4	35.4-60.7
SAM 1095	YtGFL	L-Ser (b-	YtGFL L-Ser (b-Glc) CONH2-(SE	EQ ID NO.23)	2.37	7.63	1.56	33.83	0.02	11.4	8.5-15.2
MMP 2120	YtGFL	L-Ser (a-	YtGFL L-Ser (a-Man) CONH2 (SEQ ID NO:24	3EQ ID NO:24)	22.95	15.2	3.029	23.25	0.04	31.6	26.5-37.8
MMP 2200	YtGFL	L-Ser (b-	L-Ser (b-Lactose) CONH2-	2 (SEQ ID NO:25)	17.3	40	5.727	34.75	0.02	3.2	2.5-4.2
MMP 2205	YtGFL	L-Ser, L-	L-Ser, L-Ser (b-Glc) CON	TH2 (SEQ ID NO:26)			1.169	53.51	0.3	140.8	78-253.9
MMP 2230	YtGFL	L-Ser (b-	L-Ser (b-Maltose) CONH2	(SEQ ID NO:27)	98.6	30.8	1.705	52.57	0.07	~12	,
MMP 2300	YtGFL		L-Ser (b-Maltotriose) CON	H2 (SEQ ID NO:28)	3.8	15	7.73	71.73	90.0	10.9	8.5-13.9
CM 100	YtGFL		L-Ser (b-Xyl) CONH2- (SE	EQ ID NO:29)					~0.04	9.45	8.34-10.71
MD 2005	YtGFL		L-Ser (b-Melibiose) CONF	H2 (SEQ ID NO:30)	9.6	36.6			0.034	2.16	1.84-2.53
MD 100H	YtGFL	PNLBEK	PNLBEKALKS*L-CONH	12 (SEQ ID NO:31)					~0.03		
MD 105H	YtGFL		(beta-Ala)NLBEKALKS*I	*L-CONH2 (SEQ ID NO:3 ;	3) 47.3	62.1			~0.03		
MD 110H	YtGFL	GGNLB	GGNLBEKALKS*L-CON	NH2 (SEQ ID NO:33)	35	81			~0.03		